Primary Analysis Results of the Phase 3 Archway Trial of the Port Delivery System With Ranibizumab for Patients With Neovascular AMD

Presented at Retina Society 2020

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Port Delivery System
with ranibizumab

Archway

Disclosures

Financial Disclosures

- CCA: Advisory Board: Allegro; Consultant: ArcticDx, Bausch + Lomb, Genentech, Inc., Katalyst, Volk; Stockholder: ArcticDx, Katalyst; Other: Allergan, Bausch + Lomb, Genentech, Inc.; Investigator: Adverum, Apellis, Genentech, Inc., GlaxoSmithKline, Hoffmann-La Roche, Kodiak, Merck, Mylan, Ophthotech, PanOptica, Regeneron, Stealth BioTherapeutics
- NS, DK, DK, SP, SG, GB: Employee: Genentech, Inc.

Study Disclosures

- This study includes research conducted on human subjects
- Institutional Review Board approval was obtained prior to study initiation
- Funding was provided by Genentech, Inc., a member of the Roche Group, for the study and third-party writing assistance, which was provided by Betsy C. Taylor, PhD, CMPP, of Envision Pharma Group

Archway Met Primary Endpoint: PDS Q24W Equivalent to Monthly Ranibizumab

Equivalent Vision, Controlled Retinal Thickness

- PDS noninferior and equivalent for BCVA change at weeks 36/40
- PDS controlled retinal thickness as well as monthly ranibizumab through week 40

Treatment Durability, Reduced Treatment Burden

- 98% of PDS patients did not receive supplemental treatment before first refill-exchange
- ~5x fewer treatments through week 40 for PDS patients

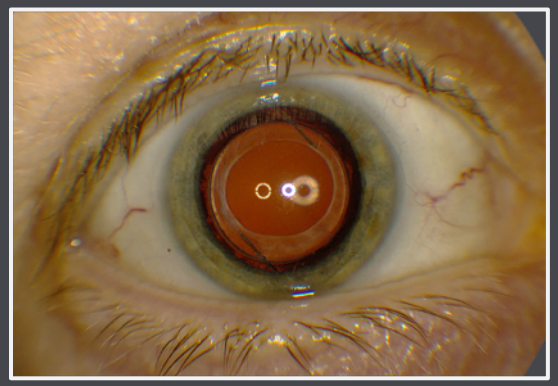
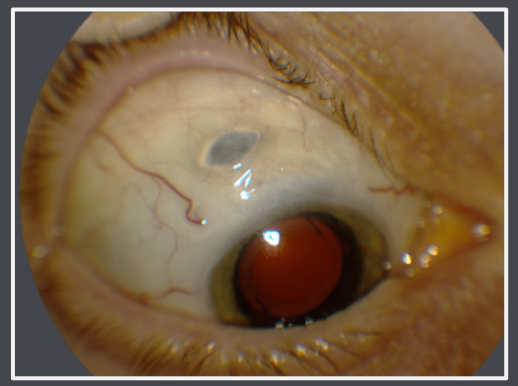
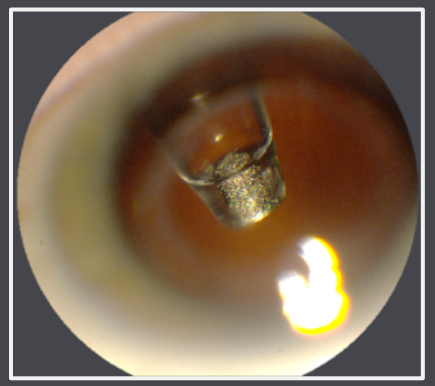
Favorable Benefit-Risk Profile

- PDS surgery-device-drug combination was generally well tolerated

BCVA, best-corrected visual acuity; PDS, Port Delivery System with ranibizumab; Q24W, every 24 weeks.

The Port Delivery System With Ranibizumab (PDS)

Continuous intravitreal delivery of a customized formulation of ranibizumab

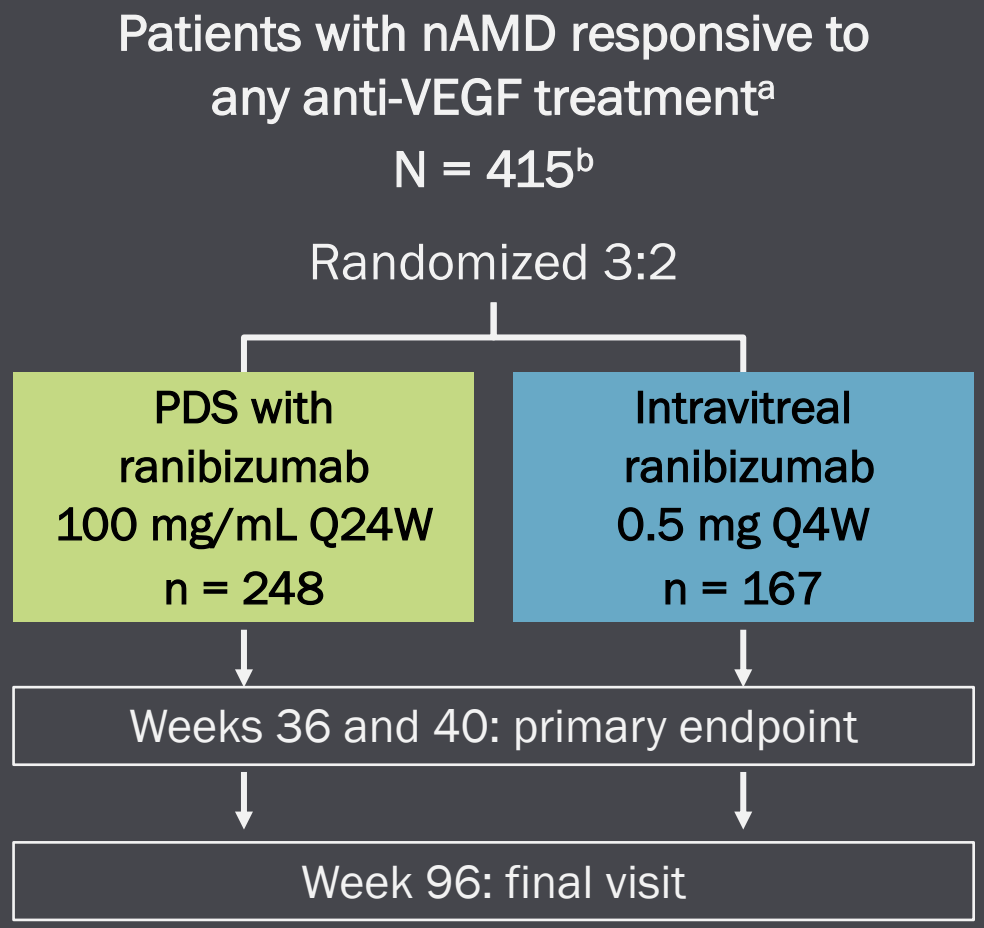





Innovative, investigational drug delivery system

- Permanent, refillable intraocular implant
- Customized formulation of ranibizumab
- Implant surgically placed at the pars plana
- In-office refill-exchange procedures

PDS, Port Delivery System with ranibizumab.

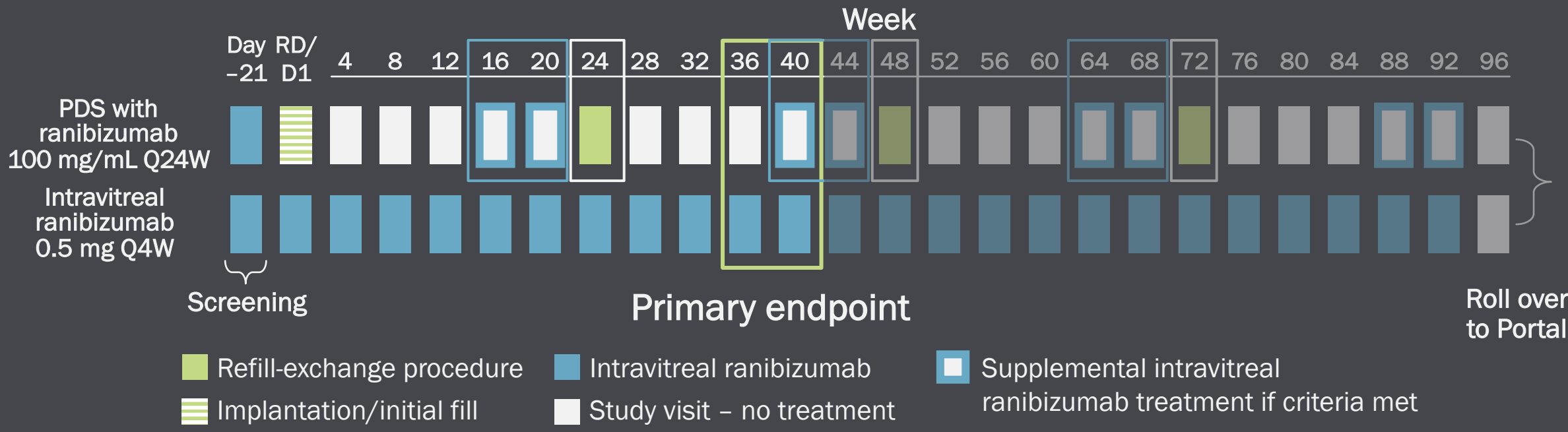
Archway: Designed to Evaluate the Efficacy and Safety of the PDS for the Treatment of nAMD



Primary objective	Evaluate noninferiority and equivalence of PDS 100 mg/mL Q24W versus intravitreal ranibizumab 0.5 mg Q4W
Primary endpoint	Change in BCVA score from baseline averaged over weeks 36 and 40

[a] nAMD in study eye diagnosed within 9 months of screening; ≥ 3 intravitreal injections of any anti-VEGF agent within previous 6 months. [b] Efficacy- and safety-evaluable population. 418 total patients were enrolled, with 251 and 167 patients randomized to the PDS 100 mg/mL Q24W and intravitreal ranibizumab 0.5 mg Q4W arms, respectively; 3 patients in the PDS arm did not receive study treatment and were excluded from the efficacy- and safety-evaluable population.
Archway, NCT03677934.
BCVA, best-corrected visual acuity; nAMD, neovascular age-related macular degeneration; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks; VEGF, vascular endothelial growth factor.

Archway Treatment Regimen: PDS With Fixed 24-Week Refill-Exchanges



Criteria for Supplemental Intravitreal Ranibizumab: Disease Activity Due to nAMD[a]				
CST + BCVA		BCVA		CST
Increase of ≥ 100 µm on SD-OCT from lowest measurement and decrease of ≥ 10 letters from best recorded score	or	Decrease of ≥ 15 letters from best recorded score	or	Increase of ≥ 150 µm on SD-OCT from lowest measurement

[a] Eligible for supplemental intravitreal ranibizumab treatment with open-label intravitreal ranibizumab at weeks 16 and 20 (after implant insertion) and at weeks 40, 44, 64, 68, 88, and 92 if any of the 3 criteria were met.
BCVA, best-corrected visual acuity; CST, central subfield thickness; D, day; nAMD, neovascular age-related macular degeneration; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks; RD, randomization; SD-OCT, spectral domain optical coherence tomography.

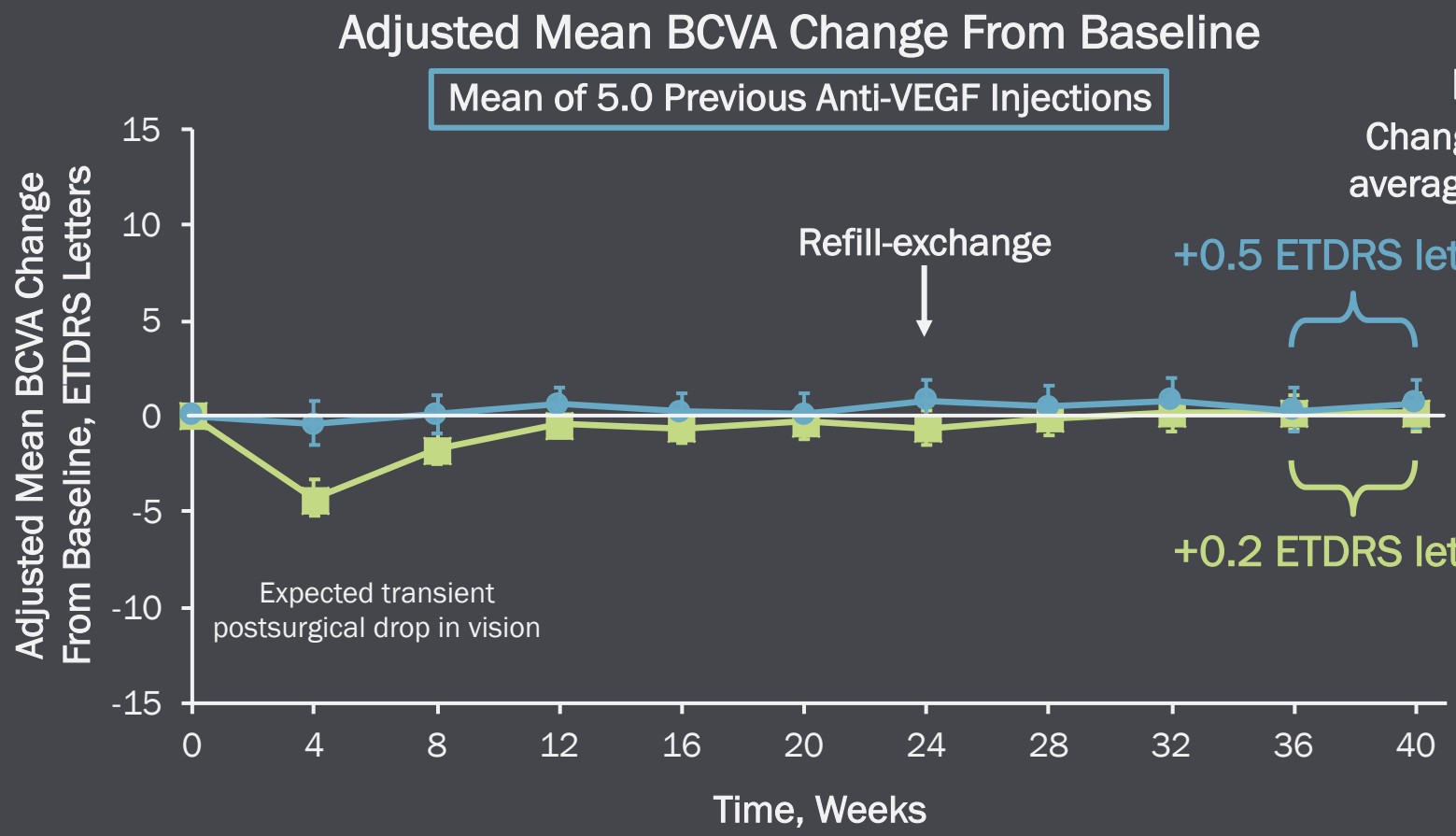
Baseline Demographics and Ocular Characteristics Were Well Balanced Across Treatment Arms

Characteristic	PDS With Ranibizumab 100 mg/mL Q24W (n = 248)	Intravitreal Ranibizumab 0.5 mg Q4W (n = 167)
Age, years		
Mean (SD)	75.2 (8.1)	74.8 (7.6)
Range	51–96	54–89
Sex, n (%)		
Male	41.5	40.1
Baseline BCVA, ETDRS letter score		
Mean (SD)	74.4 (10.5)	75.5 (10.3)
Snellen equivalent	20/32	20/32
Baseline CPT, µm		
Mean (SD)	176.9 (54.8)	177.2 (49.1)
Time since nAMD diagnosis, months		
Mean (SD)	5.9 (9.5)	5.3 (2.0)
Number of prior anti-VEGF injections		
Mean (SD)	5.0 (2.1)	5.0 (1.5)

98% study retention through week 40; no impact due to COVID-19

CPT measured from inner limiting membrane to the inner third of the retinal pigment epithelium.
BCVA, best-corrected visual acuity; CPT, center point thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; nAMD, neovascular age-related macular degeneration; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks; VEGF, vascular endothelial growth factor.

Primary Endpoint: PDS Q24W Was Noninferior and Equivalent to Monthly Ranibizumab



Primary endpoint:
Change in BCVA from baseline averaged over weeks 36 and 40

Difference in adjusted means, 95% CI

–0.3 (–1.7, +1.1)

PDS equivalent to monthly treatment

Adjusted means from a mixed-effect model for repeated measures (MMRM) analysis and vertical bars represent 95% CI. 95% CI is a rounding of 95.03% CI; the type 1 error was adjusted for interim safety monitoring. Adjusted means estimated using a MMRM with adjustment for change from baseline in BCVA as the response and included terms for treatment group, visit, treatment-by-visit interaction, and baseline BCVA (< 74 ETDRS letters vs ≥ 74 ETDRS letters).
BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks; VEGF, vascular endothelial growth factor.

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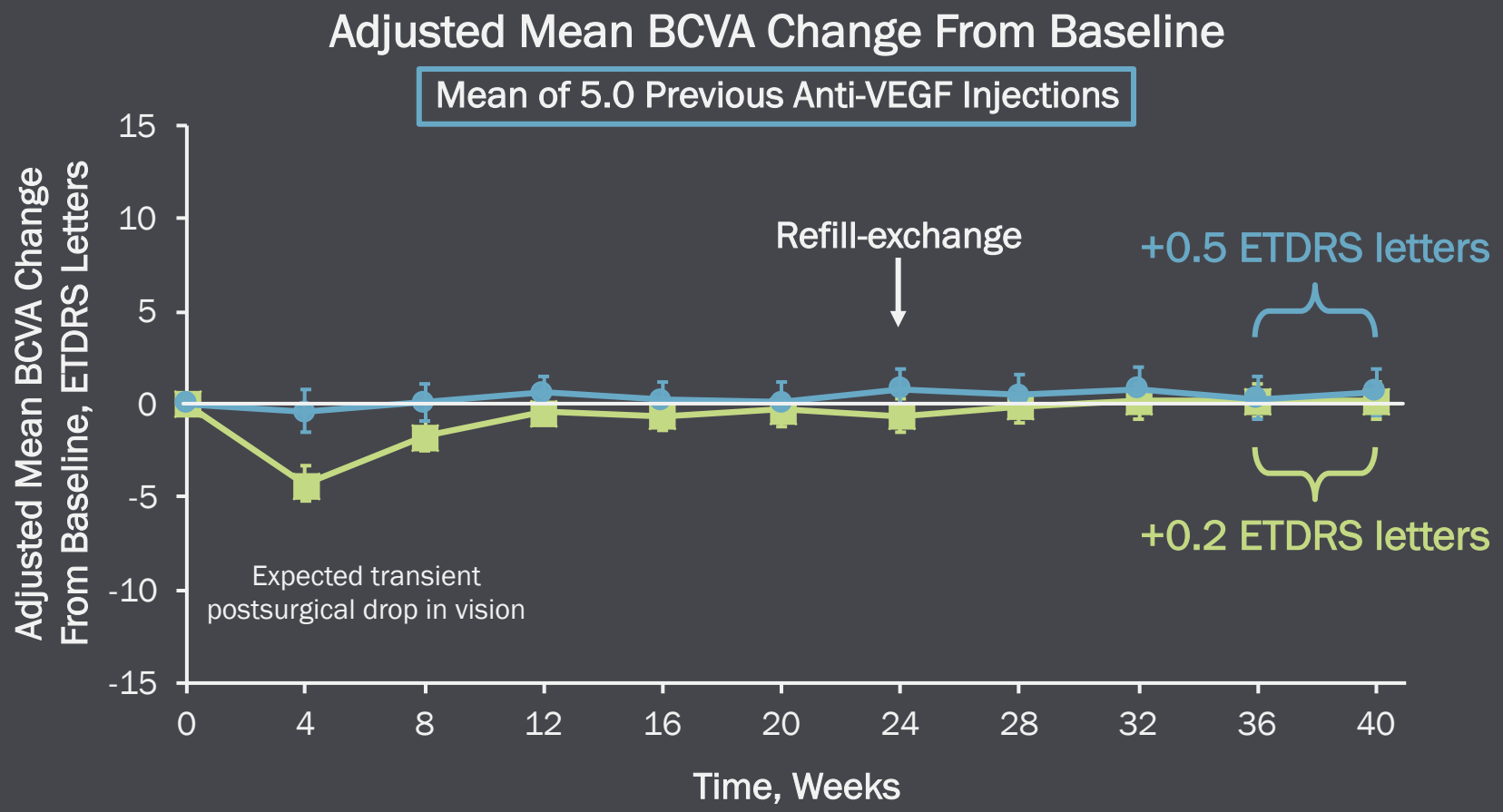
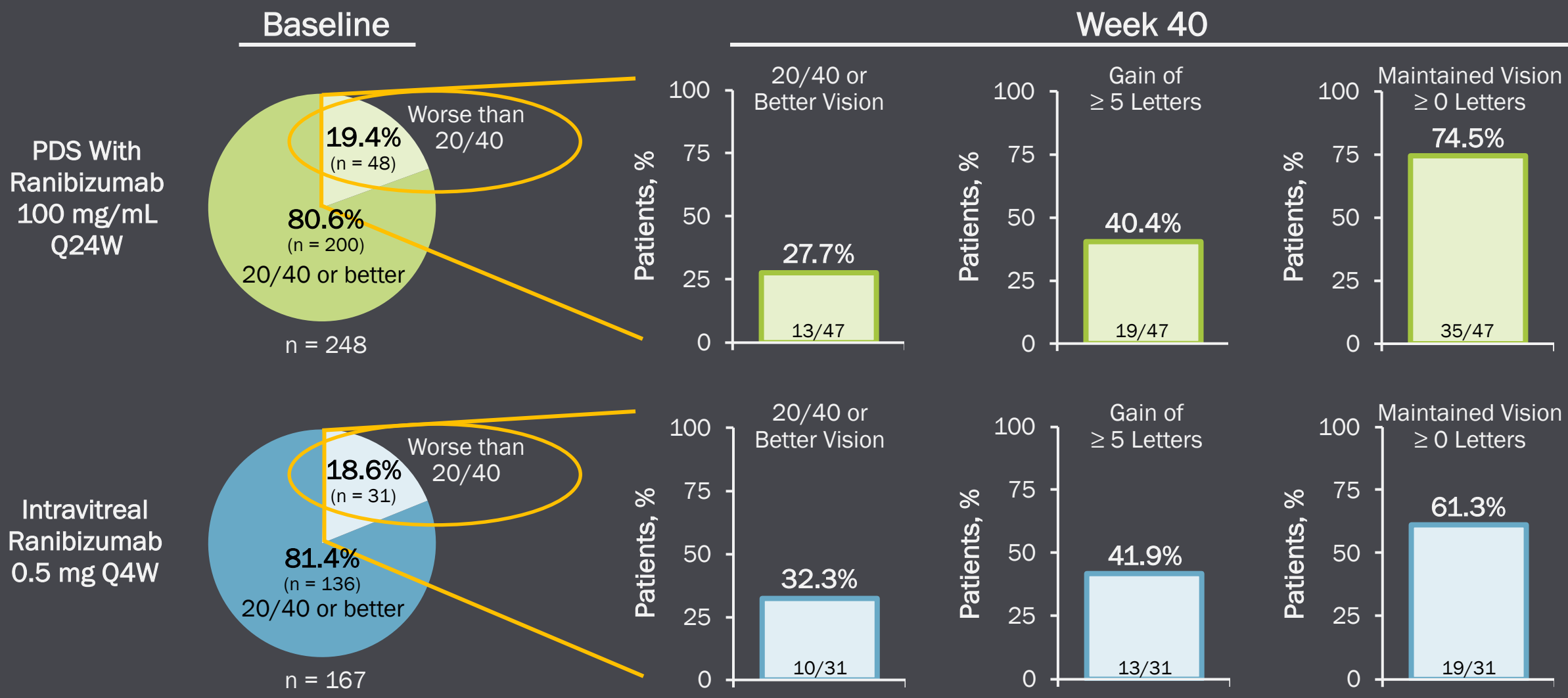


Baseline		Weeks 36/40	
ETDRS	Snellen	ETDRS	Snellen
74.4	20/32	74.6	20/32
75.5	20/32	76.0	20/32

PDS maintained vision over 40 weeks

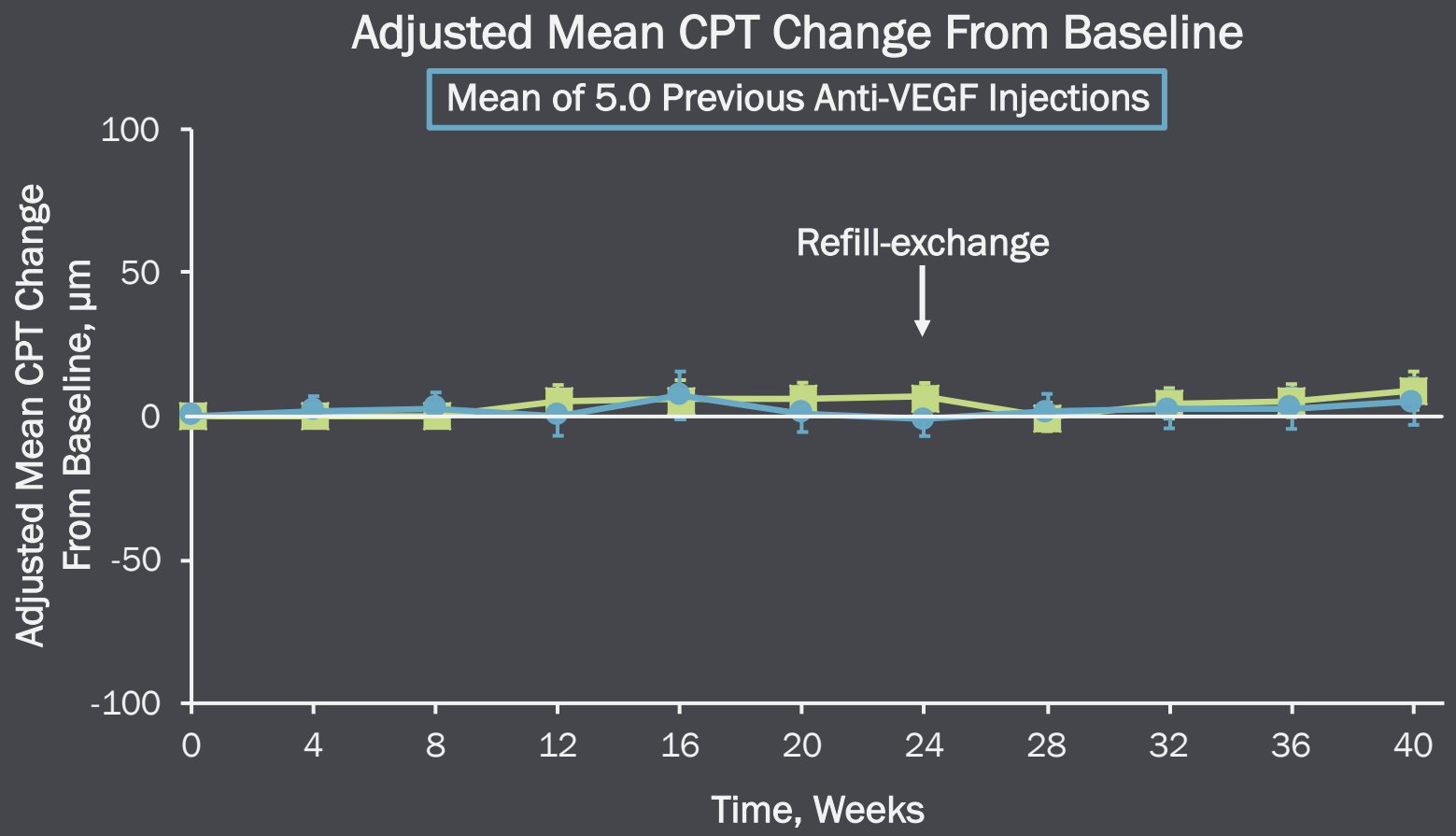
Adjusted means from a mixed-effect model for repeated measures (MMRM) analysis and vertical bars represent 95% CI. 95% CI is a rounding of 95.03% CI; the type 1 error was adjusted for interim safety monitoring. Adjusted means estimated using a MMRM with adjustment for change from baseline in BCVA as the response and included terms for treatment group, visit, treatment-by-visit interaction, and baseline BCVA (< 74 ETDRS letters vs ≥ 74 ETDRS letters).
BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks; VEGF, vascular endothelial growth factor.

PDS Patients With Baseline BCVA < 20/40 Experienced Similar Vision Gains as Monthly Ranibizumab at Week 40



BCVA, best-corrected visual acuity; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks.

PDS Controlled Retinal Thickness Through Week 40 Similar to Monthly Ranibizumab



Prespecified Secondary Endpoint, Week 36

Baseline	Week 36	Week 36 Change From BL
176.9 µm	182.3 µm	+5.4 µm
177.4 µm	180.0 µm	+2.6 µm

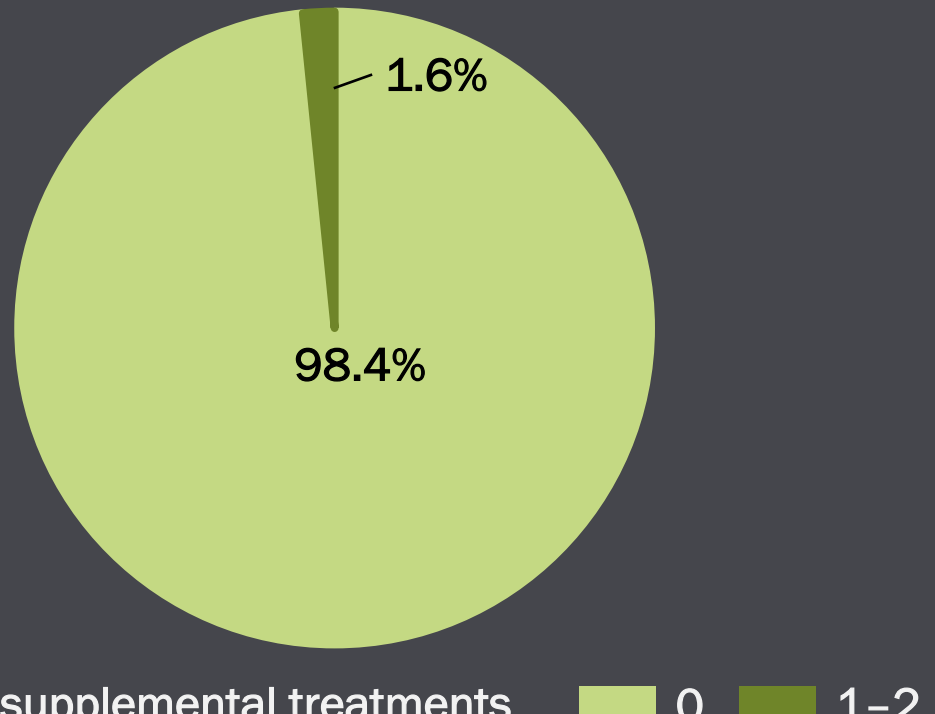
CPT defined as retinal thickness in the center of the fovea measured between the inner limiting membrane and the inner third of the retinal pigment epithelium layer. Adjusted means were estimated using a mixed-effect model for repeated measures with adjustment for change from baseline in CPT score as the response and included terms for treatment group, visit, treatment-by-visit interaction, and baseline best-corrected visual acuity (< 74 Early Treatment Diabetic Retinopathy Study [ETDRS] letters vs ≥ 74 ETDRS letters).
BL, baseline; CPT, center point thickness; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks; VEGF, vascular endothelial growth factor.

~98% of PDS-Treated Patients Did Not Receive Supplemental Treatment During First Refill-Exchange Interval

Percentage of PDS Patients Who Received Supplemental Treatment Before First Refill-Exchange at Week 24

PDS-treated patients : 248
PDS-treated patients who discontinued before first refill-exchange: 6
PDS-treated patients who received first refill-exchange: 242

- Received supplemental treatment before first refill-exchange: 4
- No supplemental treatment before first refill-exchange: 238



~5x fewer treatments through week 40 for PDS patients

PDS, Port Delivery System with ranibizumab.

Serious Nonocular AEs Through Week 40

Systemic safety of PDS Q24W was generally comparable with monthly ranibizumab

MedDRA Preferred Term, n (%)	PDS With Ranibizumab 100 mg/mL Q24W (n = 248)	Intravitreal Ranibizumab 0.5 mg Q4W (n = 167)
Total number of patients with ≥ 1 AE	28 (11.3%)	16 (9.6%)
Overall total number of AEs	36	24
Pneumonia[a]	3 (1.2%)	0
Urinary tract infection	2 (0.8%)	1 (0.6%)
Cerebrovascular accident	3 (1.2%)	1 (0.6%)
Syncope	0	2 (1.2%)
Pancreatitis	2 (0.8%)	0
Chest pain	0	2 (1.2%)
Acute respiratory failure	2 (0.8%)	0

None of the serious nonocular AEs were suspected to be related to study treatment

[a] No cases were related to COVID-19.
Observed data, safety-evaluable population who received ≥ 1 dose of study drug according to the actual treatment. Events chosen with ≥ 2 events in either arm.
AE, adverse event; MedDRA, Medical Dictionary for Regulatory Activities; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks.

Ocular Adverse Events of Special Interest[a]

PDS implant insertion and refill-exchange procedures were generally well tolerated

MedDRA Preferred Term, n (%)[b]	PDS With Ranibizumab 100 mg/mL Q24W (n			Intravitreal Ranibizumab 0.5 mg Q4W
	Time From Surger			
	≤ 1 Month	> 1 Month		
Conjunctival bleb/ conjunctival filtering bleb leak	11 (4.4%)	6 (2.4		
Vitreous hemorrhage	12 (4.8%)	1 (0.4		
Cataract[d]	1 (0.4%)	9 (3.6		
Conjunctival erosion	1 (0.4%)	5 (2.0		
Conjunctival retraction	1 (0.4%)	4 (1.6%)		
Endophthalmitis	0	4 (1.6%)	4 (1.6%)	0
Rhegmatogenous retinal detachment	1 (0.4%)	1 (0.4%)	2 (0.8%)	0
Hyphema	1 (0.4%)	0	1 (0.4%)	0

- Cases were predominantly subconjunctival thickening
- All were nonserious

All cases resolved

9 cases were addressed with flap revisions or coverage of implant flange with partial thickness cornea

- 1 of 4 cases associated with
- 3 of 4 cases vision returne baseline
- 2 of 4 patients remained on PDS treatment

2 of 2 cases repaired with vitrectomy

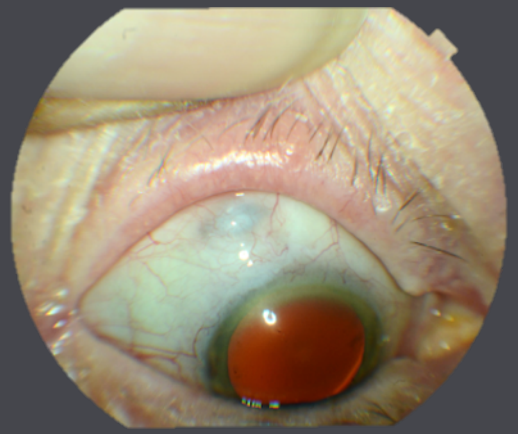
- All cases of vitreous hemorrhage resolved spontaneously – no cases required vitrectomy
- 1 of 248 PDS-treated patients had irreversible vision loss due to an adverse event (*E. faecalis* endophthalmitis)
- 1 PDS patient experienced device dislocation into the eye during a refill-exchange procedure; following removal, the patient's vision returned to baseline

[a] Protocol-defined ocular adverse events of special interest potentially related to the PDS implant or implant procedure. [b] Frequency counts by Preferred Term. Multiple occurrences of the same adverse event in an individual are counted only once for each column. [c] All data through week 40. [d] Includes the following terms: cataract, cataract nuclear, cataract cortical, cataract subcapsular. Observed data, all treated patients who received ≥ 1 dose of study drug according to the actual treatment. Month 1 visit includes data up to 37 days (monthly study visit + 7 days).
MedDRA, Medical Dictionary for Regulatory Activities; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks.

Conjunctival Bleb: Nonserious, Encapsulated Elevation of the Conjunctiva

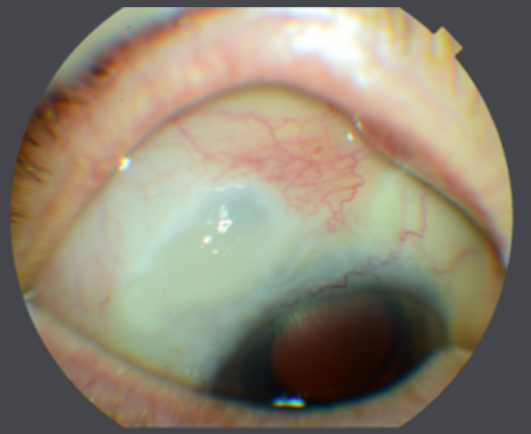
MedDRA Preferred Term, n (%)[b]	PDS With Ranibizumab 100 mg/mL Q24W (n = 248)		
	Time From Surgery		
	≤ 1 Month	> 1 Month	Total[a]
Conjunctival bleb/conjunctival filtering bleb leak	11 (4.4%)	6 (2.4%)	16 (6.5%)

Conjunctival bleb



- 15 of 16 events
- Encapsulated elevation of the conjunctiva due to thickened Tenon's capsule

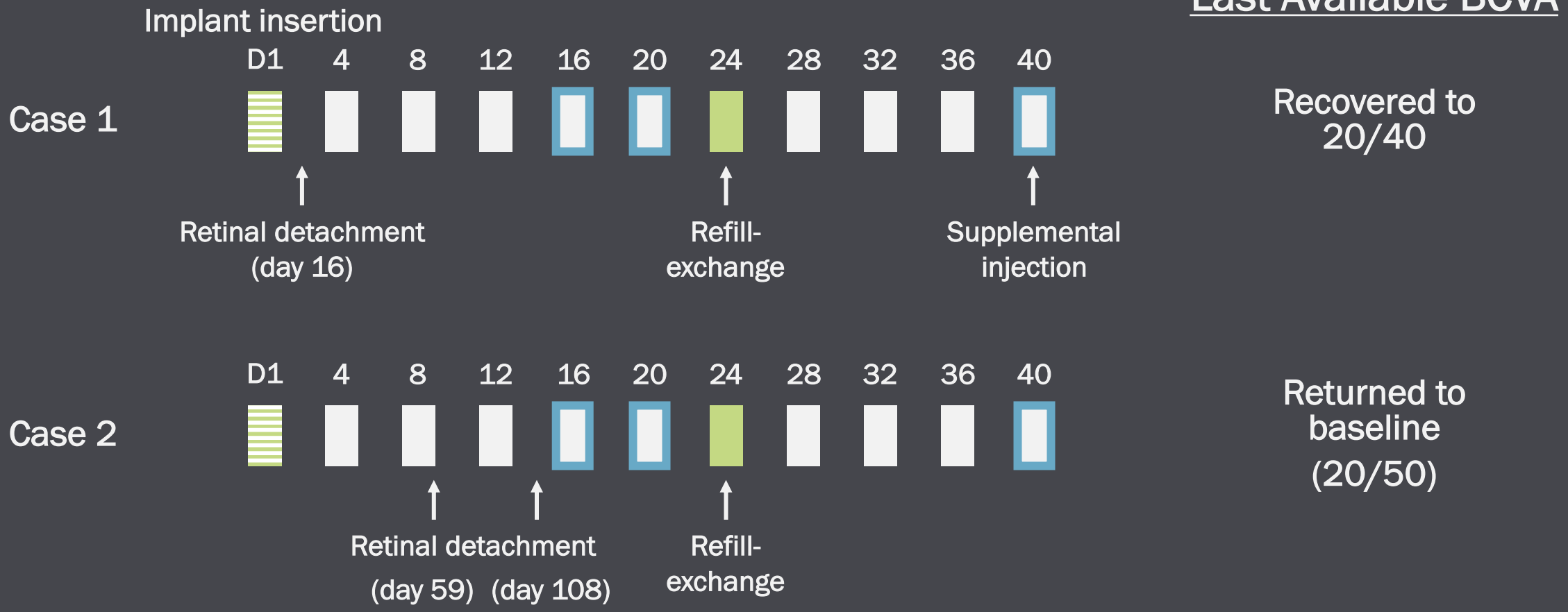
Conjunctival filtering bleb leak



- 1 of 16 events
- Elevation of conjunctiva due to fluid
- Transient and resolved without treatment

[a] All data through week 40.
MedDRA, Medical Dictionary for Regulatory Activities; PDS, Port Delivery System with ranibizumab; Q24W, every 24 weeks.

PDS Patients With Retinal Detachment Continued on PDS Treatment With Good Vision Following Vitrectomy



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- 98% of PDS patients did not receive supplemental treatment before first refill-exchange
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Favorable Benefit-Risk Profile

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PDS maintained vision while reducing treatment burden through continuous delivery of ranibizumab

BCVA, best-corrected visual acuity; PDS, Port Delivery System with ranibizumab; Q24W, every 24 weeks.

Thank You to All Participating Archway Investigators, Study Sites, and Patients

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